Mad in America
SCIENCE, PSYCHIATRY AND SOCIAL JUSTICE

Medical Journals Refuse to Retract Fraudulent Trial Reports That Omitted Suicidal Events in Children

By **Peter C. Gøtzsche, MD** - March 21, 2024

On 3 August 2023, I wrote to the editors of two medical journals and called for retraction of three fraudulent reports of placebo-controlled trials of depression drugs in children and adolescents. Ten people who lost a child or spouse to suicide as a direct consequence of being prescribed an antidepressant drug for a non-psychiatric condition were co-signatories.

The three trial reports seriously underreported suicide attempts, other suicidal events, and precursors to suicide and violence on active drug, and provided false claims that the drugs were effective.

We wrote to the editors of *Journal of the American Academy of Child & Adolescent Psychiatry* and *JAMA Psychiatry* (previously *Archives of General Psychiatry*) that,

"By retracting the fraudulent trial reports and explaining why in accompanying editorials, you will provide a much-needed service to the scientific community and the world's citizens, which will reduce the risk of additional meaningless suicides in children and young people. If you don't act, you will not only sully the reputation of your journals. You will also be seen as being complicit in future suicides caused by antidepressants as a direct harm of these drugs."

We provided trial evidence that antidepressants not only increase the *risk* of suicide but also increase *actual suicides*, even in adults. We cited research based on the clinical study reports the manufactures had submitted to drug regulators to get their drugs approved for children and adolescents and other research in our letter.

Two fraudulent fluoxetine trials

There were two fraudulent fluoxetine trials in depression. I reviewed the clinical study reports and other research extensively and published my observations with David Healy as co-author.[1]

None of the two peer-reviewed publications, which had Graham Emslie as first author,[2,3]

described the suicidal events that were mentioned in the clinical study reports, X065 and HCJE, respectively.[4,5] I asked Emslie and the manufacturer, Eli Lilly, if they wanted to restore the trials. Emslie did not reply, and Lilly did not believe that “any additional analyses are needed at this time.”

The fraud was grave. In trial X065,[4] 2 of 48 children (4%) attempted suicide on fluoxetine, but these suicide attempts were left out from the published report.

The clinical study report for trial X065 revealed that 32 of 48 children on fluoxetine versus 18 of 48 children on placebo experienced at least one adverse event (P = 0.008); 19 versus 6 experienced restlessness (P = 0.005), 9 versus 1 had nightmares (P = 0.02), and 7 versus 4 felt tense inside. These harms increase the risk of suicide and violence, but the published article did not present any such data. Only 49 words in the Results section were related to safety and it was only about discontinued children.

The efficacy analyses were also seriously flawed in favour of fluoxetine and there were numerical discrepancies that amounted to mathematical impossibilities. Despite this, the benefits, as measured by the psychiatrists, were so small that they lacked clinical significance, and the children found fluoxetine ineffective. Emslie et al. concluded in their published trial report of study X065 that fluoxetine is safe and effective, but the truth is that fluoxetine is unsafe and ineffective.

The fraud was also grave for trial HCJE, in which 109 children or adolescents with depression were randomised to fluoxetine and 110 to placebo. The clinical study report revealed that more children on fluoxetine than on placebo experienced severe adverse events to such an extent that, for every 10 children treated with fluoxetine, one was severely harmed. Nine versus 5 children had severe problems with sitting still, which Eli Lilly did not comment on although it could mean akathisia.

After 19 weeks, 42 children on fluoxetine versus 28 on placebo had experienced nervous system events (P = 0.01). By treating only 6 children with fluoxetine instead of placebo, one additional child will be harmed. Fluoxetine reduced the increases in height and weight by 1.0 cm and 1.1 kg, respectively (P = 0.008 for both). There were no data about these important harms in the published article.

In the clinical study report, Lilly concluded that fluoxetine is safe and praised its benefits and lack of harms, with no mention that the children did not find fluoxetine effective.

Taking the two studies together, adverse events definitely predisposing to violence against self or others leading to discontinuation occurred in 11 versus 3

children.

One of the strongest precursors for violence against self or others is akathisia. In an exploratory analysis that included akathisia and other potentially related symptoms, there were 37 versus 32 such adverse events in trial X065 and 51 versus 24 after 19 weeks in trial HCJE.

In the published trial report of study HCJE, Emslie et al. concluded that fluoxetine appears to be well tolerated and effective. This is blatantly false. Fluoxetine was badly tolerated and ineffective.

When the FDA assessed Lilly's application for treatment of children and adolescents with fluoxetine, they included a table of discontinuations because of adverse events in X065, HCJE and HCJW, which was a trial of obsessive-compulsive disorder comparing fluoxetine with placebo for 13 weeks in 71 versus 32 children. There were 14 versus 3 discontinuations (P = 0.02) among the 228 versus 190 children for reasons related to suicide and violence (suicide attempt, euphoria, manic reaction, agitation, hyperkinesia, nervousness, personality disorder, hostility, and depression).[1,6] There were 3 suicide attempts on fluoxetine and 1 on placebo, and another child on fluoxetine was hospitalised because of suicidality. Six children on fluoxetine developed mania or hypomania versus none on placebo (P = 0.03). A table of spontaneously reported adverse events in HCJW and HCJE (9 weeks data) showed that more children developed hyperkinesia on fluoxetine than on placebo, 12 versus 1 children (P = 0.008). This is a serious harm, as akathisia is often miscoded as hyperkinesia.[7]

A fraudulent paroxetine trial

In study 329 by Martin Keller et al., 93 adolescents with depression were randomised to paroxetine and 87 to placebo in an 8-week period (a third group received imipramine).[8]

In the published report, Keller et al. concluded that paroxetine is generally well tolerated and effective. It was neither of this. Independent researchers who had access to the clinical study report[9] and additional data found very different results.[10]

Keller et al. reported that 5 versus 1 children had suicidal or self-injurious behaviours whereas the independent researchers found 11 versus 1 children (P = 0.005). Keller et al. and the clinical study report by SmithKline Beecham had mostly misreported suicide related events as "emotional lability."

The independent researchers found that 32 versus 6 children had adverse events deemed serious by the investigators (P = 0.000006) and that 14 versus 6 children withdrew from the trial because of adverse events. Keller et al. reported that only 9 versus 6 children withdrew from the trial because of adverse events.

The independent researchers found that the efficacy of paroxetine was not statistically or clinically significantly different from placebo for any prespecified primary or secondary efficacy outcome. But changes were made post-hoc to some of the outcomes, both before and after breaking the blind, without being stated in any of the protocol amendments or in the published article, whereby they became statistically significant. This is fraud.

The reactions

On 21 September 2023, Anette Flanagin, Executive Managing Editor, Vice President, Editorial Operations *JAMA* and *JAMA Network*, sent this reply:

"We shared your letter with the author of the study published in *Archives of General Psychiatry* and he does not identify any new concerns. Similarly, we do not find new evidence in support of your request to retract this article."

So, *JAMA* and Emslie, who omitted two suicide attempts on fluoxetine and made numerous other errors, do not think this is something to bother about. Flanagin asked the person responsible for the fraud of his views and when he says there is nothing wrong, she accepts this, even though we had demonstrated the fraud. I wonder if Flanagin would recommend this method for the police when they investigate serious crime dangerous for persons.

We kindly asked Flanagin, in the public interest, to reconsider her decision not to retract Emslie's paper. And, if she still didn't want to do this, then publish an erratum explaining that what was published was seriously misleading and that many of the numbers presented in the article contrasted with the numbers in Eli

Lilly's clinical study report about the same trial. We also asked Flanagin to give us the opportunity to publish an account of the many errors in Emslie's article, asking him to respond in the same issue. Finally, we asked Flanagin to forward to us Emslie's reply to her where he indicates that there is nothing to be concerned about in his article.

We emphasised it was Flanagin's ethical duty towards the children and their relatives to do this, and that she might also want to avoid *JAMA Psychiatry* to be seen as being complicit in future suicides caused by antidepressants as a direct harm of the drugs. In our letter to Flanagin, we provided a link to the clinical study report so that she could check for herself that two suicide attempts had been left out of the published report.

Flanagin did not respond. When I contacted the journal's owner, Elsevier, they did not engage with our concerns but directed me back to the journal.

On 13 February 2024, Douglas K. Novins, Editor-in-Chief, *Journal of the American Academy of Child & Adolescent Psychiatry* (*JCAAP*), wrote to me:

"Following guidelines developed by the Committee on Publication Ethics (COPE), independent groups comprised of members of the JAACAP senior editorial team have now thoroughly reviewed your critique, as well as the responses provided by the papers' authors. We are satisfied that the critiques of the papers as outlined do not merit retraction."

I sent a similar message to Novins as my appeal to Flanagin but he did not reply.

It is hard to see how Novins could have followed the guidelines developed by the Committee on Publication Ethics (COPE), as the two trial reports, by Emslie and Keller, are clearly fraudulent.

In 2009, Leemon McHenry and Jon Jureidini wrote to the then editor of *JAACAP*, Dr. Andrés Martin, and asked him to retract study 329, as it violated the journal's own rules about scientific misconduct:

Failure to disclose financial conflict of interests; GSK's intent to deceive

(concealing commercially damaging data) via the ghost authoring company; fabrication (creation of a false primary outcome measure); falsification (misrepresentation of primary and secondary measures and serious adverse events); and plagiarism (insofar as submitting a ghostwritten manuscript is a form of plagiarism).

In 2011, McHenry and Jureidini informed all the 22 authors of study 329 of the fraud and asked them to write to *JAACAP* to have the paper withdrawn, or at least to withdraw their own names as authors. They also, with many co-signatories, wrote to President Ruth J. Simmons from Brown University where Keller worked alerting her to the serious breach of the university's own rules, noting that the unretracted article is a stain on Brown University's reputation for academic excellence, and asking her to write to *JAACAP* supporting their request for retraction.

In 2012, the editor-in-chief of *JAACAP*, Andrés Martin, wrote to Jureidini: "Following the June 27, 2012 settlement between GlaxoSmithKline and the U.S. Department of Justice, the Journal's editorial team undertook a thorough evaluation of the article, the legal settlement, and related materials. The authors of the article were contacted and asked to respond to the questions and concerns raised by the settlement. After a comprehensive and extensive review, the Journal editors found no basis for retraction or other editorial action. Due to the nature of the concerns and serious consideration given to the situation, the evaluation process was quite lengthy, and we appreciate your patience while the editorial team conducted its review. The inquiry is considered complete, and as such, your letter will not be published in the Journal."

In 2013, The Executive Committee of the Northern California Regional Organization of Child and Adolescent Psychiatry wrote a letter to the Ethics Committee at the American Academy of Child and Adolescent Psychiatry, the owner of *JAACAP*. They noted that FDA's Clinical Review of study 329 considered it a failed trial, in that neither active treatment group showed superiority over placebo. But publicly, study 329 was called "cutting edge research" demonstrating "REMARKABLE" results, and by 2010, there were an estimated 184 citings of the paper in the medical literature, suggesting its widespread influence.

The Executive Committee noted it was troubling that the journal has not retracted "the demonstratedly fraudulent article" and that three of the members were told that the Ethics Committee was instructed *not* to investigate the paper. They formally requested that the Ethics Committee conduct a full investigation and furthermore noted:

"There is nothing in our By-Laws to prevent such an investigation. In fact, the Mission of the Academy encourages it: 'To promote the healthy development of children, adolescents, and families through research, training, advocacy, prevention, comprehensive diagnosis, and treatment.'"

Absolutely nothing came out of their initiative either. They were fobbed off with a lecture about "editorial independence" and a patronising dismissal: "I have talked with [the Editor] and he assures me there is no cause for concern."

A fraudulent citalopram trial

In 2004, Karen Wagner et al. published a fraudulent trial report in *American Journal of Psychiatry* owned by the American Psychiatric Association.[11] It claimed that citalopram significantly improved depressive symptoms compared with placebo in children and adolescents.

But the drug was not better than placebo. The evidence for misreporting and data manipulation was revealed in a class action lawsuit, The Celexa and Lexapro Marketing and Sales Practice Litigation, and published by Jay Amsterdam, Jon Jureidini and Leemon McHenry in 2016.[12]

The manuscript was ghostwritten, and Forest Laboratories, Lundbeck's US partner, seriously misrepresented both the effectiveness and the safety of citalopram. Forest's internal documents showed that company staff were aware of the problems. Contrary to the study protocol, children that should have been excluded were included in the analyses to produce statistical significance for the primary outcome measure; an implausibly large effect size was claimed, which was subsequently proven wrong; positive post hoc outcomes were introduced while negative primary and secondary outcomes were not reported; and adverse events were misleadingly analysed, hiding substantial agitation in the citalopram group.

Declassified court documents revealed that Forest intentionally misled the FDA about study protocol violations that invalidated the claim that the study was positive.

In 2016, Amsterdam, Jureidini and McHenry asked Wagner to write to the editor and request him to retract the paper, or at least to withdraw her own name from the article. She didn't reply.

They asked the current editor, Robert Freedman, to retract the article. When he refused, they asked the editor who accepted the paper, Nancy Andreasen, to support retraction of the article, but she didn't reply.

They also informed Maria A. Oquendo, President of the American Psychiatric Association, about the scientific misconduct and asked her to take action. She didn't reply.

Absolutely nothing was done.

Consequences of the fraudulent trials

The consequences of the fraudulent trials are huge, and the fraud is not limited to trials of fluoxetine, paroxetine, and citalopram.[7] They are all over the place in this area but these drugs just happened to be the ones where the fraud has been most closely examined.

When my research group did a systematic review of placebo-controlled antidepressant trials (all ages) based on clinical study reports, we also found highly disturbing data.[13] For children and adolescents, the odds ratios were 2.39 (95% confidence interval 1.31 to 4.33) for suicidality, 2.79 (1.62 to 4.81) for aggression, and 2.15 (0.48 to 9.65) for akathisia (which was underreported because of miscoding).

Patient narratives were only available for serious events and for aggression. They included homicidal threat, homicidal ideation, assault, sexual molestation, a threat to take a gun to school, damage to property, punching household items, aggressive assault, verbally abusive and aggressive threats, and belligerence. Such harms are not likely to ever appear in published trial reports.

It is a fatal mistake to believe that antidepressants are safe and effective. Many children and young people who were driven to suicide by the harms of the antidepressant they took did not even have a condition that justified the prescription, e.g. their problem could be insomnia, stress at work, anxiety before a school exam, or break-up with a girlfriend.[7]

It is characteristic for antidepressant induced suicide that people choose highly violent means, e.g. hanging or shooting.[7] They feel so terrible because of the harms of the pills that they want to ensure they will end their lives. In contrast, people who attempt suicide because of depression often use other means, e.g. an overdose of pills, which gives them a chance of surviving and is usually a cry for help.

Prestigious psychiatric journals, psychiatrist investigators and professional organisations do not live up to their academic and ethical responsibilities. They seem to be totally reckless, as they don't care that their activities make them complicit in suicides among children and in harming them in numerous other ways with drugs that don't work for them. None of the many authors on the fraudulent trial reports have asked to have their name removed.

A 2022 meta-analysis of placebo-controlled trials funded by industry that included 6161 children and adolescents found a tiny effect size, only 0.12, using the Children's Depression Rating Scale-Revised (CDRS-R).[14] An effect this small does not have any clinical meaning.[7] We therefore know with great certainty that depression pills do not work for depression in young people. But they double their risk of suicide.[15,16]

We should stop publishing in psychiatric journals. They are too corrupted by financial and other conflicts of interest, which is one among several reasons why some of us now prefer to publish on websites where there is no censorship.[17] Psychiatric journals constitute what three US child and adolescent psychiatrists that were appalled by the ubiquitous corruption called "Liars' club."

It is disgraceful that children are treated with depression drugs. This should be made illegal and the companies and the psychiatric journals should be sued for consumer fraud with lethal consequences.

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Peter C. Gøtzsche, MD has published more than 100 papers in the top five general medical journals and his scientific works have been cited over 150,000 times. He has published several books relevant to psychiatry, including *Deadly Psychiatry and Organised Denial*, *Mental Health Survival Kit and Withdrawal from Psychiatric Drugs*, and *Critical Psychiatry Textbook*. He is currently crowdfunding for his Institute for Scientific Freedom with the goal of preserving honesty and integrity in science.